REMARKS

Claims 1, 2, 5-8, 9-13, 15, 18-35, and 37-50 were pending. Claim 1 has been amended to only clarify the virus like particle comprises the multiple membrane spanning protein of interest. Claims 1, 2, and 5-8, and 50 are under examination.

No new matter has been added.

Summary of the Invention:

As an aid to the Office, Applicants believe that a summary of the invention may be beneficial. The present invention is directed to a composition that can be used, for example, to study the properties/functions of a multiple membrane spanning protein (*i.e.* a protein that spans the membrane more than once) and to identify compounds that can modulate the function of the multiple membrane spanning protein in an isolated particle in such a way that was not possible prior to the present invention, (*i.e.*, in their native confirmation; prior methods did not allow this confirmation).

The present invention overcomes the difficulties of studying a multiple membrane spanning protein of interest by producing a composition that can incorporate ***any*** multiple membrane spanning protein of interest into the particles (*i.e.*, a lipoparticle or virus-like particle) in a native confirmation.

The present invention can be applied to any multiple membrane spanning protein because the specific multiple membrane protein that is incorporated into the virus-like particle is not the invention, but rather the invention allows one of ordinary of skill in the art to study and manipulate multiple membrane spanning proteins of interest in an environment (a virus-like particle) that wasn't possible prior to the present invention. Applicants' invention is not the discovery of multiple membrane spanning proteins but, rather, the incorporation of the same in virus-like particles. The specific identity of the multiple membrane spanning protein is not what is important but rather that they can now be produced and studied in a virus-like particle.

Rejection under 35 U.S.C. § 112

Claims 1, 2, 5-8, and 50 were rejected under 35 U.S.C. § 112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Office alleges that the claims are

> broadly directed toward a virus-like particle comprising an enveloped virus core comprising multiple membrane spanning proteins of interest. The only limitation on the membrane spanning protein of interest is a negative limitation that specifies that the protein is not CD63. However, the claims do not provide any positive claim limitations that further define the inserted protein.

(Office Action, page 2). Applicants traverse this rejection.

As an initial matter, Applicants would like to reiterate, as stated in a previous communication to the Office and discussed during a previous interview with the Examiner, the case law cited by the Office in support of this rejection is not relevant to the pending claims in the present application. The cases cited by the Office are directed, *inter alia*, to written description defects in claims directed to nucleic acid sequences of genes that have not been cloned and to chemical sub-genuses that were not described. Neither of these fact patterns apply to the present invention. The present invention is not directed to nucleic acid sequences or chemical sub-genuses. Instead, as discussed below, more current case law is applicable to the present invention, which supports Applicants' position that the claims satisfy the written description requirement.

The claims do, in fact, provide positive limitations that define the inserted protein. Claim 1, for example, describes the protein as being a multiple membrane spanning protein. Therefore, the positive limitation is that the protein must span the membrane more than once, otherwise the protein would not be a multiple membrane spanning protein. Claim 8 describes seven specific multiple membrane spanning proteins. Therefore, Applicants respectfully assert that the Office's allegation that the claims do not provide any positive limitations that further define the inserted protein is incorrect.

The Office also alleges that the specification "fails to prove any further illumination on the structure of the protein." (Office Action, page 4). Applicants respectfully submit that such is not necessary. Applicants desire to encompass ***all*** membrane spanning proteins within the claim scope, not a particular membrane spanning protein or a sub-set of same. In that regard, the Office's comment that the disclosure fails to lead the skilled artisan to any particular membrane spanning protein is factually incorrect and irrelevant, as is the Office's reliance upon *Fujikawi v. Wattanasin*. Indeed, the Office's argument would be germane if Applicants were trying to claim a particular membrane spanning protein, or sub-set of membrane spanning proteins, not disclosed in the specification. Such is not the case.

The Office appears to argue that the Applicants are required to provide the structure of any multiple membrane spanning proteins that are to be incorporated into the virus-like particle. The Office relies on the decision of *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997), *inter alia*, to support this apparent requirement. Applicants respectfully assert that the Examiner is misapplying the case law to the present application.

As discussed in Applicants previous response, and again here for emphasis, the present invention is not dissimilar to *Capon v. Eshhar* where the Federal Circuit overturned the Board of Patent Appeals and Interferences ("Board") rejection of claims for lack of written description. See *Capon v. Eshhar*, 418 F.3d 1349, 1359-1360, (Fed. Cir. 2005). In *Capon,* the claims recited chimeric DNAs (or genes) comprising DNA encoding , for example, a single chain Fv domain of a specific antibody and the transmembrane and cytoplasmic domain of an endogenous protein. *Id. at* 1352-1353. The Board had rejected such claims for lack of written description, arguing that novel genetic material was being described in terms of the functional characteristics of the protein encoded. *Id.* at 1354-1355. The Board, relying upon much of the same precedent relied upon by the Office in rejecting Applicants' claims, was requiring the complete sequence. *Id.*

In response, the parties argued, *inter alia*, that the chimeric genes are produced by selecting and combining known DNA segments, using known procedures. *Id.*, at 1355. Notably, the Board did not dispute that persons in the field could determine the structure or formula from

the known structure or formula of the components. *Id.* The Federal Circuit observed that none of the cases relied upon by the Board required a re-description of what was already known. *Id.*, at 1357-1358. The court stated,

> The "written description" requirement must be applied in the context of the particular invention and the state of the knowledge. . . .When the prior art includes the [allegedly lacking] information, precedent does not set a per se rule that the information must be determined afresh.

Id., 1358. In the present case, as in *Capon*, the individual components were known.

Capon was recently cited approvingly in another Federal Circuit decision regarding written description. In *Falkner v. Inglis*, 05-1324, (Fed. Cir., May 26, 2006), the losing party in the interference argued that the claims did not satisfy the written description requirement because the Application did not provide the sequences of the essential genes of the Poxvirus, had not produce a vaccine based without the essential genes of the poxvirus, and that the specification was directed not to poxvirus but to a different type of virus. *Id.* at *p.6. Notably, the Board properly rejected these arguments, finding writing descriptive support. The Federal Circuit agreed and held that

> [I]n accordance with our prior case law, that (1) examples are not necessary to support the adequacy of a written description (2) the written description requirement may be met...even where actual reduction to practice of an invention is absent; and (3) ***there is no per se rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure.***

Id. at *p. 14, emphasis added.

The present application satisfies the written description requirement of 35 U.S.C § 112 because not only does the present application provide examples, but Applicants also reduced many of them to practice. The *Falkner* decision reinforces and emphasizes that there is no rule that the application must contain a recitation of a sequence of every biological macromolecule when the molecules are known to one of skill in the art.

The sequences of every known multiple membrane spanning protein are not required. "The forced recitation of known sequences in patent disclosures would only add unnecessary

bulk to the specification." *Falkner* at *p.17. The Office appears to require what the court Board and Federal Circuit deem "unnecessary." The Office's allegation that the application does not show possession is unfounded because the present invention is incorporating any multiple membrane spanning protein of interest into a virus-like particle. Applicants are not claiming the multiple membrane spanning protein itself, but rather its incorporation into a virus-like particle as described and enabled by the present application. Accordingly, a requirement to describe the sequence of every possible multiple membrane spanning protein is "unnecessary" and in not in agreement with the Federal Circuit's decisions in *Falkner* and *Capon*.

In explaining that there is no *per se* rule to describe what is already known, such as the sequences of multiple membrane spanning proteins, *Falkner* quoted *Capon*, where the court stated

> The descriptive text needed to meet these requirements varies with the nature and scope of the invention at issue, and with the scientific and technologic knowledge already in existence. The law must be applied to each invention that enters the patent process, for each patented advance is novel in relation to the state of the science. Since the law is applied to each invention in view of the state of relevant knowledge, its application will vary with differences in the state of knowledge in the field and differences in the predictability of the science.

Falkner at *.p17, *Capon* at 1357. Here, the state of the art at the time the present application was filed was such that one of skill in the art would understand what is meant by a multiple membrane spanning protein of interest. And, information regarding particular structures, etc., is clearly provided in the accessible literature. The inclusion of the sequences of every multiple membrane spanning protein of interest is not required. *See Faulkner* at *17.

Regardless, Applicants have amply complied with the Office's written description requirements. As set forth in M.P.E.P. § 2163 the written description for a claimed genus can be satisfied by sufficient description of a representative number of species by 1) actual reduction to practice; 2) reduction to drawings; 3) by disclosure of relevant identifying characteristics, *e.g.* structure; ***or*** 4) a combination of the foregoing. The Office has only focused upon the third basis.

The specification as filed sufficiently describes multiple membrane spanning proteins. First, a structure is provided. Applicants respectfully direct the Office's attention to page 59, beginning at line 7, where a multiple membrane spanning protein is described as a polypeptide that spans the cell membrane at least twice. Thus, contrary to the Office' assertion the protein is not without structure.

Second, the specification discloses various types of multiple membrane spanning proteins. Numerous divergent multiple membrane spanning proteins are described on page 62, beginning at line 5, of the specification. The specification discloses, for example, multiple membrane spanning proteins such as G-protein coupled receptors (*e.g.*, mu-opioid receptors), as well as transporters (proteins that transport molecules such as, but not limited to, amino acids or carbohydrates, across a membrane), ion channels, and the like. The specification also discloses the actual reduction to practice of virus-like particles comprising divergent multiple membrane spanning proteins, for example, the specification discloses a virus-like particle comprising the amino acid transporter (and MLV receptor) MCAT-1 (see, page 63, beginning at line 18) and virus-like particles comprising the G protein-coupled receptors CXCR4 or CCR5 (see, Example 3, page 78, beginning at line 15). Similar to *Capon* and *Falkner*, Applicants' invention is not the discovery of multiple membrane spanning proteins but, rather, the incorporation of the same in virus-like particles. *See Capon* at 1358, *Falkner* at *p.13.

The present claims and specification constitute "more than a wish for possession" or a "laundry list" as the Office alleges. (Office Action, page 4, 5). In contrast to the cases cited by the Office, the present application discloses the incorporation of a diverse set of multiple membrane proteins into virus-like particles such that one of ordinary skill in the art would recognize that the Applicants were in possession of the genus at the time the application was filed. One of ordinary skill in the art would be able to use the present invention to incorporate ***any*** multiple membrane spanning protein of interest into a virus-like particle as described in the pending claims.

Accordingly, the skilled artisan would consider that Applicants were in possession of the claimed invention at the time of filing. Applicants have demonstrated possession by describing virus-like particles comprising a variety of multiple membrane spanning proteins.

Thus, for the reasons set forth above, Applicants respectfully submit that the specification as filed provides sufficient written description for the claims as presently amended, and, therefore, respectfully request reconsideration and withdrawal of the rejection of the claims under 35 U.S.C. § 112, first paragraph.

Conclusion

Applicants believe the claims are in condition for allowance. An early Notice of Allowance is therefore earnestly solicited. Applicants invite the Examiner to contact the undersigned at (215) 665-6928 to clarify any unresolved issues raised by this response.

Respectfully submitted,

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